

CLAIMS

1. A method of inhibiting inflammation in a subject in need thereof, comprising contacting cells of the subject with an active agent that induces up-regulation of RUNX3 expression in the cells.
- 5 2. The method of claim 1 wherein the cells are selected from thymocytes and dendritic cells (DC).
3. The method of claim 2 wherein the cells of the subject are dendritic cells (DC).
4. The method of claim 3 wherein the active agent reduces the proportion of mature DC versus immature DC in said subject.
- 10 5. The method of claim 4, wherein the reduction in the proportion of mature DC versus immature DC is determined by a reduction in the proportion of DC expressing CD80, CD86, MHC class II and OX40L.
6. The method of claim 1, wherein the active agent comprises a polynucleotide encoding Runx3 or encoding a RUNX3 promoter activator.
- 15 7. The method of claim 6 wherein the polynucleotide construct further comprises a viral-based vector.
8. The method of claim 1 wherein the contact between the cells and the active agent is performed *ex vivo*.
9. The method of claim 1, wherein the subject suffers from disorder selected from a chronic inflammatory disease, a T cell-mediated autoimmune disease or tissue transplantation.
- 20 10. A method of inhibiting T cell proliferation in a subject in need thereof, comprising contacting cells of the subject with an active agent that induces up-regulation of RUNX3 expression, thereby inhibiting the T cell proliferation.
- 25 11. The method of claim 10 wherein the cells are dendritic cells.

12. The method of claim 11 wherein the agent reduces the proportion of mature DC versus immature DC in said subject, thereby inhibiting DC mediated T-cell proliferation.
- 5 13. A method of attenuating DC maturation in a subject in need thereof, comprising contacting DC of the subject with an active agent that induces up-regulation of RUNX3 expression in the DC, thereby attenuating the DC maturation in said subject.
- 10 14. A method for enhancing T cell-mediated immune response in a subject in need thereof, comprising contacting cells with an active agent that down-regulates the expression of RUNX3 in the cells, thereby enhancing the T cell-mediated immune response in the subject.
- 15 15. The method of claim 14 wherein the cells are dendritic cells.
16. The method of claim 15 wherein the agent increases the proportion of mature DC versus immature DC.
- 15 17. The method of claim 16, wherein the increase in the proportion of mature DC versus immature DC is determined by the increase in the proportion of DC expressing CD80, CD86, MHC class II and OX40L.
- 20 18. The method of claim 14, wherein the active agent comprises an antisense nucleotide specific for RUNX3 mRNA molecules, thereby down-regulating the expression of RUNX3 in the cells.
19. The method of claim 14, wherein the contact between the DC and the active agent is performed *ex vivo*.
- 25 20. The method of claim 14, wherein the subject in need suffers from a disorder selected from a tumor and an infectious disease, the infectious disease caused by a pathogen, a bacteria, a virus, a fungus and a parasite.
21. A method of testing the efficacy of a treatment for a chronic inflammatory disease comprising subjecting a mouse that is homozygous for a RUNX3 null allele to a putative treatment and determining the efficacy of said treatment by

measuring the severity of symptoms characteristic of said disease exhibited by said mouse, in comparison to the severity of symptoms exhibited by the same mice not exposed to the treatment.

22. The method of claim 21, wherein said chronic inflammatory disease is
5 selected from: a eosinophilic lung inflammation-related disease, a chronic obstructive pulmonary disease and an inflammatory bowel disease.
23. The method of claim 22, wherein said chronic obstructive pulmonary disease is chronic bronchitis.
24. The method of claim 22, wherein said eosinophilic lung inflammation-related
10 disease is acute bronchial asthma.
25. The method of claim 22, wherein said inflammatory bowel disease is Crohn's disease or ulcerative colitis.
26. The method of claim 22, wherein the severity of symptoms associated with
15 said eosinophilic lung inflammation-related disease or chronic obstructive pulmonary disease is quantitated by at least one of: an increase in the CD4⁺ subset of T lymphocytes and a decrease in the CD8⁺ T lymphocytes, eosinophilic infiltration in the lung, increased levels of IL-5 and increased CD11c+/CD11b+ DC/macrophage subset in bronchoalveolar lavage, compared to wild type mice at the RUNX3 locus.
- 20 27. The method of claim 22, wherein the symptoms of said inflammatory bowel disease comprise at least one of: typhlocolitis, gastric mucosal hyperplasia, proliferative gastritis and proximal duodenitis.
28. The method of claim 22, further comprising subjecting said mouse to environmental agents prior to the treatment, said agents inducing exacerbation
25 of the symptoms of the disease.
29. A method of predicting an increased risk for a chronic inflammatory disease in a subject comprising the steps of: (a) obtaining a test sample from the subject to be assessed; and (b) determining the expression of RUNX3 in the sample, wherein when the expression of RUNX3 in said test sample is diminished

compared to normal levels expressed in healthy subjects, said subject has an increased risk of susceptibility to a chronic inflammatory disease.

30. The method of claim 29, wherein said chronic inflammatory disease is an eosinophilic lung inflammation-related disease, a chronic obstructive pulmonary disease or an inflammatory bowel disease.
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31. The method of claim 29, wherein the expression of RUNX3 is determined by measuring the level of mRNA specific for the RUNX3 gene or the level of the Runx3 protein.
32. The method of claim 29, wherein the test sample is obtained from peripheral blood mononuclear cells (PBMC).
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33. The method of claim 30, wherein said chronic obstructive pulmonary disease is chronic bronchitis.
34. The method of claim 30, wherein said eosinophilic lung inflammation-related disease is acute bronchial asthma.
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35. The method of claim 30, wherein said inflammatory bowel disease is Crohn's disease or ulcerative colitis
36. The method of claim 31 wherein the level of mRNA specific for the RUNX3 gene is measured by Northern blot, in situ hybridization or RT-PCR.
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37. The method of claim 32 wherein the level of the Runx3 protein is measured by ELISA, radioimmunoassay, western blot or immunohistochemistry.
38. The method of claim 29, wherein said subject is a human subject.
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39. A method of testing the efficacy of a treatment for a chronic inflammatory disease comprising subjecting cells derived from a knockout mouse that is homozygous for a RUNX3 null allele to a putative treatment in vitro and determining the efficacy of said treatment.

40. The method of claim 39, wherein the chronic inflammatory disease is selected from: an eosinophilic lung inflammation-related disease, a chronic obstructive pulmonary disease and an inflammatory bowel disease.
41. The method of claim 39, wherein the cells are DC.
- 5 42. The method of claim 41, wherein the efficacy of said treatment is determined by measuring the proportion of mature DC versus immature DC.
- 10 43. The method of claim 42 wherein the efficacy of said treatment is determined by measuring the proportion of DC expressing at least one of CD80, CD86, MHC class II and OX40L, wherein the treatment is effective against the chronic inflammatory disease if there is a reduction in the proportion of DC expressing at least one of CD80, CD86, MHC class II and OX40L.
- 15 44. A kit for diagnosis of genetic susceptibility to a chronic inflammatory disease comprising at least one probe capable of determining at least one genotype associated with the RUNX3 gene, or the expression of the gene product encoded by this locus.
45. The kit of claim 44 wherein the probe is adapted for determining at least one SNP associated with the RUNX3 gene.
46. A pharmaceutical composition comprising a polynucleotide construct encoding RUNX3 or a RUNX3 promoter activator.
- 20 47. A pharmaceutical composition comprising a viral vector comprising the construct according to claim 46.
48. A pharmaceutical composition comprising a polynucleotide that down regulates expression of Runx3.